REMARKS

The Immature Finality of the Office Action

Applicants respectfully submit that the Examiner prematurely issued a Final Office Action in this case, based on the following facts:

- As part of the Examiner's Restriction Requirement mailed 12/07/05 the Examiner required Applicants to select a species. The Restriction Requirement went on to state: "...upon election of a single compound the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound..." (Restriction Requirement, page 3, lines 20-22). Moreover, the Restriction Requirement further went on to provide: "A clear statement of the examined invention... will be set forth in the first action on the merits. **Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds ... under examination.**" (Restriction Requirement, page 4, lines 7-11) (emphasis added).
- In the first action on the merits, mailed 4/13/06, the Examiner first set forth his self-determined "scope of the invention", which limited the examined subject matter to compounds in which, *inter alia*, "R^3 is a 6-membered ring with ring members consisting of only carbon and nitrogen, optionally substituted as defined, optionally unsaturated as defined;" (4/13/06 Office Action, page 3, lines 1-3). The Examiner went on to state: "As a result of the election and the corresponding scope of the invention defined supra, the remaining subject matter of Claims 1-12, 16-19, 23-27, 29-30, 32, 34 and 36 are withdrawn from further consideration ... as being drawn to non-elected inventions." (4/13/06 Office Action, page 3, lines 5-8.)
- In their response to the first action on the merits, filed 8/11/ Applicants traversed the Examiner's self-determined "scope of the invention" which constituted such an integral part of the Restriction Requirement, and which was revealed to Applicants for the first time in the 4/13/06 Office Action. Specifically, it was stated: "Applicants respectfully submit that the

Examiner's limitation of R^3 is not consistent with the language of the claims at issue. Specifically, the words **"6 membered ring with ring members consisting of only carbon and nitrogen..."** appear nowhere in the specification or claims, and their insertion into the claims raises potential issues of new matter. At a minimum, Applicants are entitled to a limitation of R^3 that speaks in the same terms of that originally contained in the specification and claims. In this case, Applicants have used the term: **"substituted or unsubstituted 5-6 membered heterocyclyl..."**.and Applicants submit that the use of these terms is more appropriate than the language that has been constructed, Ex parte , by the Examiner.

- The Examiner never responded to Applicants' traversal, and never stated that the Restriction Requirement had been made final.

As a result of the foregoing facts, there is significant uncertainty as to the scope of the invention currently being examined. For example, where the Examiner states in the pending Final Office Action: "Claims 1-3, 5-7, 9-11, 17, 19-20, 23, 24, 29, 30-32, 34 and 36 are objected to for containing elected and non-elected subject matter" (Final Action, page 4, lines 1-2), it is unclear if the Examiner is intending that a complete response to the action requires Applicants to amend the definition of R^3 to conform to the original "scope of the invention" set forth in the first action on the merits. Applicants have not entered such an amendment herein, because they believe the limitation would be improper, and the Restriction Requirement was never made final.

Claims Withdrawn from Consideration

The Final Office Action provides that claims 21, 22, 28, 35 and 37-45 have been withdrawn from consideration. In response Applicants have herein canceled these claims.

Applicants respectfully submit, however, that since the amendments presented herein place the elected composition claims in condition for allowance, canceled method

claims 37-45 are properly subject to rejoinder as they are dependent upon allowable claims.

Previous Claim Objections

The Final Office Action provides that the Examiner objects to claims 1-3, 5-7, 9-11, 17, 19, 23, 24, 29, 30, 32, 34, and 36 on the basis that non-elected subject matter remains for R^2 (see Final Office Action at page 2, lines 16-17).

Applicants submit that the objection is improper as the "scope of the invention" set forth by the Examiner in the first action on the merits, contains absolutely no limitation on the scope of R^2 (see 4/13/06 Office Action at page 2, line 15 to page 3, line 4). Alternatively, Applicants request that the Examiner clarify the basis of these objections.

Previous Claim Rejections - 35 USC § 102

The Examiner has maintained the previous rejection of claims 1-4, 10-12, 16-17, 19, 23-25, 29 and 36 as being anticipated by Huth et al. (WO 00/27819) on the basis that the previous amendment failed to fully exclude 1,2,3,4-tetrahydroquinolyl. Applicants have herein amended claims 1 and 2 to delete the generic term "tetrahydroinolinyl", and submit that this amendment obviates the rejection.

Current Claim Objections

The Examiner has objected to claims 1-3, 5-7, 9-11, 17, 19-20, 23, 24, 29, 30-32, 34 and 36 "for containing elected and non-elected subject matter. The elected subject matter have been identified supra." (Final Office Action at page 4, lines 1-3). To the extent that the objection is based on the Examiner's previous objection to the scope of R^2 (see Final Office Action at page 2, lines 16-17), Applicant's submit that the rejection is improper as the "scope of the invention" set forth by the Examiner in the first action on the merits, contains absolutely no limitation on the scope of R^2 (see 4/13/06 Office Action at page 2, line 15 to page 3, line 4). Alternatively, Applicants request that the Examiner clarify the basis of these objections.

In order to try to fully respond to the action, and place the claims in better form for appeal, Applicants have amended the claims to limit the claims to elected subject matter--as Applicants understand what the proper elected subject matter actually is in this case. Specifically, Applicants have:

- Amended claim 2 to delete the proviso appearing at the end of the claim--which only applies to cases where R^1 is a phenyl group (which is outside the scope of the definition of R^1);
- Amended claim 5 to delete the term "4,4-dimethyl-2-oxo-1,2,3,4-tetrahydroquinol-7-yl", as this term does not find an antecedent basis in the definition of R^1 in claim 2;
- Amended claim 17 to delete the term "(3-pyridyl)-$(CH_2)_2$-" as this term does not find an antecedent basis in the definition of R in claim 2; and
- Amend claim 30 to delete the compound "N-{4-[1-Methyl-1-(1-methyl-piperidin-4-yl)-ethyl]-phenyl}-2-[(pyridin-4-ylmethyl)-amino]-benzamide".

The Examiner has also objected to claims 3 and 9 as being of improper dependent form for failing to further limit the subject matter of the previous claim. Applicants have herein canceled claims 3 and 9 in order to obviate the rejection.

Current Claim Rejection - 35 USC § 102

The Examiner has rejected claims 1-3, 10-11, 17, 19-20, 23-24, 29 and 36 as being anticipated by Huth et al. (WO 00/27819). Applicants submit that the amendments entered herein to claims 1 and 2 to delete the generic term "tetrahydroinolinyl", obviate the current claim rejection under 35 USC § 102.

Current Rejections Under 35 USC § 103

The Examiner has raised a series of rejections based on 35 USC § 103. Applicants address each of them below in detail:

Huth et al., Patani et al., and In re Wood

The Examiner has rejected claims 30 and 34 as being unpatentable over Huth et al. (WO 00/27819) in view of Patani et al. (Chem. Rev. 1996, 3147,3176) and of In re Wood (199 USPQ 137). Applicants respectfully submit that the Examiner has failed to make a prima facie case of obviousness.

In describing the disclosure of Huth et al., the Examiner properly notes that this reference does not disclose (1) the substitution of pyrimidine for pyridene in the R^3 group; (2) the substitution of tetrahydroisoquinolyl for tetrahydroquinolyl in the R^1; or (3) methyl groups on the tetrahydroquinolyl of R^1.

To fill in these missing gaps the Examiner relies on:

- Patani et al. (pp. 3158-3159) for the proposition that pyridine/pyrimidine, as well as quinoline/isoquinoline are equivalent structures in any and all cases; and
- In re Wood for the proposition that hydrogen and methyl are obvious variants.

Applicants respectfully submit that the Examiner has interpreted the teaching of Patani et al. far to broadly, and that a fair consideration of this reference does not actually provide a prima facie case of obviousness for the substitution of pyrimidine for pyridine or the substitution of isoquinoline for quinoline in this instance. Indeed, a review of the pages of Patani et al. specifically cited by Examiner reveals that this disclosure does not even encompass the substitution of pyrimidine for pyridine, or the substitution of isoquinoline for quinoline. Rather, these pages disclose, *at best*, that:

(1) in relation to antihistamine effect, certain pyridines and phenyls can be employed to obtain active compounds (see Figure 31 at p. 3158), and

(2) in relation to antibacterial effect, certain quinilones and isoquinolones can be employed to obtain active compounds (see Figure 38 at p. 3159).

The other ring systems discussed at pages 3158-3159 of Patani et al., do not even approach structural similarity between pyridines/pyrimidones or quinolines/isoquinolines. The Examiner's belief that this disclosure of Patani et al. clearly establishes that any substitution of N for CH in any aromatic systems (or NH for CH_2 in any non-aromatic systems) will always result in compounds of equivalent activity in all targets, is simply an overreaching interpretation that is not supported by the disclosure itself. Indeed Patani et al. specifically note that:

- "The concept of bioisoseterism is often considered to be qualitative and intuitive." (Patani et al. at page 3147), rather than the facile, precise, all-encompassing generalizations than have been put forth by the Examiner.

- The substitutions discussed in the reference only represent *potential* for producing compounds of similar activity. (See page 3148: "Thus, an additional objective of this review was to demonstrate *the opportunities* that one has in employing bioisosteres" (emphasis added); and "Bioisosteric replacements of functional groups ... have enhanced *the potential* for the successful development of new clinical agents" (emphasis added); See also page 3158: "Classical isosteric substitutions when applied within ring systems result in different heterocyclic analogues which *can be* effective bioisoteres."). Thus, it is clear that Patani et al. do not purport to endorse the type of broad interpretation that has been set forth by the Examiner, in an attempt to support this rejection. At best, Patani et al. provide a suggestion **to try** isosteric substitutions in order to find bioisosteric equivalents in relation to certain targets. Patani, et al. do not even attempt to suggest that such substitutions will always work in any target at issue.

The Examiner's extremely overbroad interpretation of Patani et al. represents the foundation of the obviousness rejection. The failure of the Patani reference to actually suggest the propositions set forth by the Examiner, causes the rest of the analysis to fall.

Huth et al., Patani et al. Fotouhi et al., and In re Wood

The Examiner has rejected claims 5-7, and 9 as being unpatentable over Huth et al. (WO 00/27819), Patani et al. (Chem. Rev. 1996, 3147,3176), Fotouhi et al. (US 2002/0052512, and of In re Wood (199 USPQ 137). Citing the same pages of Patani et al., the Examiner states that the reference establishes that 5-yl and 6-yl indoles, as well as quinolines/isoquinolines, are equivalent structures. Again, a review of the specific pages cited by the Examiner reveals that the reference does not even approach a discussion of equivalency between 5-yl and 6-yl indoles. In order support this proposition the Examiner, again, has to rely on an overly broad interpretation of the reference that assumes that any substitution of N for CH in any aromatic systems (or NH for CH_2 in any non-aromatic systems) will always result in compounds of equivalent activity in all targets. For all the reasons discussed above, this interpretation is not supportable, and accordingly the rejection falls like a house of cards.

The Examiner also bases an aspect of the rejection on the breadth of the term "pharmaceutically acceptable derivatives". Applicants have herein amended the claims to replace this term with "pharmaceutically acceptable salts". Applicants submit that any concern arising from the breadth of the term "derivatives" has been obviated by the amendment.

The Examiner has also rejected claim 31 as being unpatentable over Huth et al. (WO 00/27819), in view of Patani et al. (Chem. Rev. 1996, 3147,3176), Fotouhi et al. (US 2002/0052512, and of In re Wood (199 USPQ 137). largely on the same basis as the rejection of claims 5-7 and 9 discussed above. For all the same reasons, the Examiner has failed to establish a prima facie case of obviousness.

Application No.: 10/615,809 Attorney Docket No. A-817 (US)

CONCLUSION

Applicants submit that the rejections of record have been overcome by the above Amendments and Remarks provided herein, and request that the case be passed to allowance.

Respectfully submitted,

Dated: January 19, 2007

Ronald S. Hermenau, Reg. No. 34,620
Attorney for Applicants
AMGEN INC.
1120 Veterans Boulevard
South San Francisco, CA 94080
Phone: (650) 244-2261
Fax: (650) 837-9422

RECEIVED
CENTRAL FAX CENTER

JAN 19 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Qi Huang, et al.**	Attorney Docket No. **A-817 (US)**
Application No.: **10/615,809**	Art Unit No.: **1626**
Filed: **July 8, 2003**	Examiner: **Joseph R. Kosack**
Title: **SUBSTITUTED ANTHRANILIC AMIDE DERIVATIVES AND METHODS OF USE**	

PETITION PURSUANT TO 37 C.F.R. § 1.181 TO WITHDRAW THE FINALITY OF THE PENDING ACTION

Mail Stop: After Final/Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

COPY

Sir:

Applicants respectfully submit that the Examiner has prematurely issued a Final Office Action in this case, and request that the Director withdraw the finality of the action. This petition is based on the following facts:

- As part of the Examiner's Restriction Requirement mailed 12/07/05 the Examiner required Applicants to select a species. The Restriction Requirement went on to state: "...upon election of a single compound the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound..." (Restriction Requirement, page 3, lines 20-22). Moreover, the Restriction Requirement further went on to provide: "A clear statement of the

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper (along with any referred to as being attached or enclosed) (4 pages total) is being facsimile transmitted to the United States Patent and Trademark Office, (571) 273-8300, on the date shown below:

January 19, 2007
Date

Julie M. Belot

examined invention... will be set forth in the first action on the merits. **Note that the restriction requirement will not be made final until such time as applicant is informed of the full scope of compounds ... under examination.**" (Restriction Requirement, page 4, lines 7-11) (emphasis added).

- In the first action on the merits, mailed 4/13/06, the Examiner first set forth his self-determined "scope of the invention", which limited the examined subject matter to compounds in which, *inter alia,* "R^3 is a 6-membered ring with ring members consisting of only carbon and nitrogen, optionally substituted as defined, optionally unsaturated as defined;" (4/13/06 Office Action, page 3, lines 1-3). The Examiner went on to state: "As a result of the election and the corresponding scope of the invention defined supra, the remaining subject matter of Claims 1-12, 16-19, 23-27, 29-30, 32, 34 and 36 are withdrawn from further consideration ... as being drawn to non-elected inventions." (4/13/06 Office Action, page 3, lines 5-8.)
- In their response to the first action on the merits, filed 8/11/ Applicants traversed the Examiner's self-determined "scope of the invention" which constituted such an integral part of the Restriction Requirement, and which was revealed to Applicants for the first time in the 4/13/06 Office Action. Specifically, it was stated: "Applicants respectfully submit that the Examiner's limitation of R^3 is not consistent with the language of the claims at issue. Specifically, the words **"6 membered ring with ring members consisting of only carbon and nitrogen..."** appear nowhere in the specification or claims, and their insertion into the claims raises potential issues of new matter. At a minimum, Applicants are entitled to a limitation of R^3 that speaks in the same terms of that originally contained in the specification and claims. In this case, Applicants have used the term: **"substituted or unsubstituted 5-6 membered heterocyclyl..."**.and Applicants submit that the use of these terms is more appropriate than the language that has been constructed, Ex parte , by the Examiner.
- The Examiner never responded to Applicants' traversal, and never stated that the Restriction Requirement had been made final.

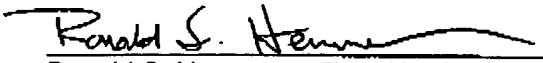
As a result of the foregoing facts, there is significant uncertainty as to the scope of the invention currently being examined. For example, where the Examiner states in the pending Final Office Action: "Claims 1-3, 5-7, 9-11, 17, 19-20, 23, 24, 29, 30-32, 34 and 36 are objected to for containing elected and non-elected subject matter" (Final Action, page 4, lines 1-2), it is unclear if the Examiner is intending that a complete response to the action requires Applicants to amend the definition of R^3 to conform to the original "scope of the invention" set forth in the first action on the merits. Applicants have not entered such an amendment herein, because they believe the limitation would be improper, and the Restriction Requirement was never made final.

As provided in Section 706.07 of the MPEP, before a final rejection can be properly made, the issues should be clearly developed between the Examiner and the Applicant. As described above, such is not the case here. Further, as provided in Section 706.07(c), questions as to the prematureness of a final rejection are petitionable under 37 C.F.R. § 1.181.

Applicants do not believe that a fee is required for the submission of this petition, as their review of 37 C.F.R. § 1.17 does not appear to contain an entry relating to petitions under 37 C.F.R. § 1.181. However, in the event that the Office determines that a fee is required for the submission of this petition, the Commissioner is hereby authorized to charge any fees due, or credit any overpayments to Deposit Account No. 01-0519.

Respectfully submitted,

Dated: January 19, 2007



Ronald S. Hermenau, Reg. No. 34,620
Attorney for Applicants
AMGEN INC.
1120 Veterans Boulevard
South San Francisco, CA 94080
Phone: (650) 244-2261
Fax: (650) 837-9422